Yellow Fever

1) THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Yellow fever is a mosquito-borne viral illness. It is caused by the yellow fever virus, which is in the genus *Flavivirus* and family *Flaviviridae*.

B. Clinical Description

Many cases of yellow fever are so mild they go undetected. In typical cases of recognized illness, the patient experiences a sudden onset of fever, chills, headache, backache, generalized muscle pain, prostration, nausea and vomiting. Jaundice, albuminuria (the presence of protein in the urine), and anuria (absence of urine) may occur. Most infections resolve at this stage. However, in more severe cases of illness, after a brief remission of hours to a day, there is progression to liver and kidney failure and to hemorrhagic symptoms, including nosebleeds, bleeding gums, bloody vomiting and bloody stools. Twenty to fifty percent of severe cases with jaundice are fatal. The overall case-fatality rate in endemic regions is about 5% percent. Lifetime immunity follows yellow fever recovery.

C. Reservoirs

Monkeys and mosquitoes are the primary reservoirs in forested areas of Africa and South America. Humans and *Aedes aegypti* mosquitoes are involved in the infective cycle in urban areas.

D. Modes of Transmission

Yellow fever has two different transmission cycles that affect humans, the urban cycle and the jungle cycle. In the urban cycle, the virus is transmitted among humans by the bite of an infective house-dwelling *Aedes aegypti* mosquito. Monkeys play little or no role as a reservoir. In the jungle cycle, several species of mosquitoes are vectors and transmit virus from monkey to monkey. Humans are involved in the jungle cycle accidentally if they are bitten by infected mosquitoes. In South America, sporadic infection of humans occurs almost exclusively in forestry and agricultural workers through occupational exposure. Direct person-to-person spread of yellow fever does not occur.

E. Incubation Period

The incubation period for yellow fever is 3 to 6 days.

F. Period of Communicability or Infectious Period

Yellow fever is not transmitted from person-to-person. The blood of patients is infective for mosquitoes from shortly before onset of fever until 3 to 5 days of illness. The incubation period in *Aedes aegypti* mosquitoes is commonly 9 to 12 days at the usual tropical temperatures. Once infected, mosquitoes remain so for life.

G. Epidemiology

Yellow fever is now endemic to certain regions of South America and Africa only. Any cases in Massachusetts are probably due to recent travel abroad.

2) REPORTING CRITERIA AND LABORATORY TESTING SERVICES

A. What to Report to the Massachusetts Department of Public Health

- Report any suspect case of yellow fever based on a healthcare provider's medical opinion or any positive laboratory result pertaining to yellow fever.

Note: See Section 3) C below for information on how to report a case.

B. Laboratory Testing Services Available

Laboratory testing for yellow fever is not available at the Massachusetts State Laboratory Institute (SLI). However, the SLI Viral Serology Laboratory will forward specimens to the Centers for Disease Control and Prevention (CDC) for yellow fever testing. CDC requests that physicians submit complete case history information with the specimens. For additional information on submitting samples, contact the Viral Serology Laboratory at (617) 983-6396.

3) DISEASE REPORTING AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To identify imported cases of yellow fever to understand the global epidemiology of endemic and epidemic yellow fever.
- To ensure that cases are appropriately contained to prevent the introduction of virus into native mosquito populations.
- To identify locally acquired cases, if they occur, so appropriate active surveillance and mosquito control interventions can be taken.
- To identify cases that may be part of a larger, worldwide outbreak.
- To provide travelers with appropriate preventive health information.

B. Laboratory and Healthcare Provider Reporting Requirements

The Massachusetts Department of Public Health (MDPH) requests that healthcare providers and laboratories report to the local board of health in the community where diagnosed all cases of yellow fever (by telephone, confidential fax or in writing) no more than 24 hours after diagnosis. A case of yellow fever is defined by the reporting criteria in Section 2) A above. Refer to the lists of reportable diseases (at the end of this manual's Introduction) for specific information.

C. Local Board of Health Reporting and Follow-Up Responsibilities

1. **Reporting Requirements**

The MDPH requests that each local board of health (LBOH) report the occurrence of any case of yellow fever, as defined by the reporting criteria in Section 2) A above to the MDPH Division of Epidemiology and Immunization, Surveillance Program using an official MDPH *Generic Disease Case Report Form* (in Appendix A). Refer to the *Local Board of Health Reporting Timeline* (at the end of this manual's introductory section) for information on prioritization and timeliness requirements of reporting and case investigation.

2. **Case Investigation**

   a. Case investigation of yellow fever in Massachusetts residents will be directed by the MDPH Division of Epidemiology and Immunization.

   b. Following notification of the MDPH, the LBOH(s) may be asked to assist in completing an official MDPH *Generic Disease Reporting Form* (in Appendix A) by interviewing the case and others who may be able to provide pertinent information. Most of the information required on the form can be obtained from the provider or the medical record. Use the following guidelines to assist you in completing the form:
      1) Record "Yellow Fever" as the disease being reported.
      2) Record the case's demographic information.
      3) Record the date of symptom onset, symptoms, date of diagnosis, hospitalization information (if applicable), and outcome of disease (*e.g.*, recovered, died).
      4) Exposure history: use the approximate incubation period range for yellow fever (3–6 days). Specifically, focus on the period beginning 3 days prior to the case's onset date back to approximately

6 days before onset for travel history: determine the date(s) and geographic area(s) traveled to by the case.

5) Complete the import status section to indicate where yellow fever was acquired. If unsure, check "Unknown."
6) Include information about the case's yellow fever vaccination status, including the date most recently vaccinated. This information can be documented in the "Comments" section.
7) Include any additional comments regarding the case.
8) If you have made several attempts to obtain case information, but have been unsuccessful (*e.g.,* the case or healthcare provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as you have gathered. Please note on the form the reason why it could not be filled out completely.

c. After completing the form, attach lab report(s) and mail (in an envelope marked "Confidential") to the MDPH Division of Epidemiology and Immunization, Surveillance Program. The mailing address is:

MDPH, Division of Epidemiology and Immunization
Surveillance Program, Room 241
305 South Street
Jamaica Plain, MA 02130

d. Institution of disease control measures is an integral part of case investigation. It is the LBOH responsibility to understand, and, if necessary, institute the control guidelines listed below in Section 4), Controlling Further Spread.

4) CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (*105 CMR 300.200*)

None.

B. Protection of Contacts of a Case

It is important to prevent mosquitoes from biting a case for at least 5 days after onset of illness. Mosquito control can be done by screening sickrooms, spraying with insecticides and using bed nets. These measures can prevent transmission of yellow fever from infected mosquitoes to contacts of a case. *Note:* The *Aedes aegypti* mosquito has not been found in Massachusetts, although it and other potential vectors are expanding their range. Concerns over local transmission should be small, however.

C. Managing Special Situations

Locally Acquired Case

As noted above in Section 4) B, a locally acquired case of yellow fever would be an unusual occurrence as the *A. aegypti* mosquito has not been found in Massachusetts. However, in recent years a resurgence of *A. aegypti* has occurred in South America and has increased the potential for reemerging urban yellow fever (see Section 1D for a description of urban fever) in the United States. If you determine during the course of an investigation that a case or suspect case does not have a recent travel history to an endemic country, contact the on-call epidemiologist at the Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850 as soon as possible. Environmental measures such as investigating local areas visited by the case to locate the focus of infection and surveillance of other people for illness may be necessary.

Reported Incidence Is Higher than Usual/Outbreak Suspected

If you suspect an outbreak, investigate to determine source of infection and mode of transmission. A common exposure to or association with *A. aegypti* mosquitoes (*e.g.,* travelers returning from endemic countries) should be sought and applicable preventive or control measures should be instituted. Contact the on-call epidemiologist at the Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850 as soon as possible. The Division can help determine a course of action to prevent further cases and can perform surveillance for cases that may cross several town lines and therefore be difficult to identify at a local level.

D. Preventive Measures

International Travel and Vaccination

- A live vaccine is recommended for all individuals over 9 months old who will be living in or traveling to endemic areas, and required by international regulations for travel to and from certain countries. Pregnant women should not be vaccinated in the first trimester except in high-risk areas.
- Without a valid certificate of immunization against yellow fever, many countries require a 6-day quarantine of travelers coming from or going to recognized yellow fever zones of Africa and South America.
- Travelers to yellow fever endemic countries are encouraged to protect themselves from mosquitoes by using repellents, wearing protective clothing and using mosquito nets when rooms are not screened. Unlike other vectors, the principal mosquito vectors of yellow fever bite during daytime hours.
- For more information regarding international travel and the yellow fever vaccine, contact the CDC's Traveler's Health Office at (877) 394-8747 or through the internet at <http://www.cdc.gov/travel>.

.

ADDITIONAL INFORMATION

The following is the formal CDC surveillance case definition for yellow fever. It is provided for your information only; it is not necessary to use this information for reporting or investigating a case. (CDC case definitions are used by the state health department and CDC to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2) A of this chapter.

Clinical description

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and symptoms and, in some instances, renal failure, shock, and generalized hemorrhages.

Laboratory criteria for diagnosis

- Fourfold or greater rise in yellow fever antibody titer in a patient who has no recent history of recent yellow fever vaccination and cross-reactions to other flaviviruses have been excluded or
- Demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid.

Case classification

Probable: a clinically compatible case with supportive serology (stable elevated antibody to yellow fever virus [*e.g.*, ≥32 by complement fixation, ≥256 by immunofluorescence assay, ≥320 by hemagglutination inhibition, ≥160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)
Confirmed: a clinically compatible case that is laboratory confirmed

REFERENCES

American Academy of Pediatrics. *1997 Red Book: Report of the Committee on Infectious Diseases, 24th Edition*. Illinois, American Academy of Pediatrics, 1997

CDC. Case Definitions for Infectious Conditions Under Public Health Surveillance, *MMWR*. 1997; 46:RR-10.

Chin, J., ed., *Control of Communicable Diseases Manual, 17th Edition.* Washington, DC, American Public Health Association, 2000.

Evans, Alfred. *Viral Infections of Humans, Epidemiology and Control, Second Edition*. New York, Plenum Medical Book Company, 1984.

Mandell, G., Bennett, J., Dolin, R., eds. *Principles and Practice of Infectious Diseases, Fourth Edition*. New York, Churchill Livingstone Inc., 1995.